IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

STEPHEN WENDELL and LISA WENDELL, as successors in interest to MAXX WENDELL, deceased,

Plaintiffs,

v.

JOHNSON & JOHNSON; CENTOCOR, INC.; ABBOTT LABORATORIES; SMITHKLINE BEECHAM d/b/a GLAXOSMITHKLINE; TEVA PHARMACEUTICALS USA; GATE PHARMACEUTICALS, a division of TEVA PHARMACEUTICALS USA; PAR PHARMACEUTICAL, INC.,

Defendants.
/

No. C 09-04124 CW

ORDER GRANTING MOTIONS FOR SUMMARY JUDGMENT (Docket Nos. 177, 179, 183 and 185)

This is a pharmaceutical product liability case in which Plaintiffs Stephen and Lisa Wendell have sued as successors-in-interest to their son, Maxx Wendell, the decedent. The Wendells allege claims for negligence and strict liability, asserting that Defendants Abbott Laboratories, GlaxoSmithKline LLC (GSK),[1] TEVA Pharmaceuticals USA, Gate Pharmaceuticals, a division of TEVA Pharmaceuticals, and PAR Pharmaceuticals, Inc. failed adequately to warn about certain risks posed by their products, specifically two prescription drugs: Humira and mercaptopurine (also known as

[1] GSK was formerly known as and erroneously served and sued in this action as SmithKline Beecham d/b/a GlaxoSmithKline.

6-mercaptopurine, 6-MP and Purinethol). These Defendants have each separately moved for summary judgment, arguing that the Wendells cannot show evidence of proximate causation necessary to establish liability for failure to warn. Docket Nos. 177, 179, 183 and 185. Having considered all of the parties' submissions and oral argument, the Court GRANTS the motions.

BACKGROUND

Abbott is the alleged manufacturer, marketer and distributor of Humira in California. GSK and TEVA are purportedly the manufacturers, and the California marketers and distributors of 6-MP, sold under the brand name Purinethol. PAR is allegedly a manufacturer, marketer and distributor of 6-MP in California. The Wendells have also sued Johnson & Johnson and its wholly owned subsidiary, Centocor, Inc., both of which are allegedly involved in the manufacture, marketing, sale and distribution of Remicade. Johnson & Johnson and Centocor have not moved for summary judgment.

In the fall of 1998, Maxx was diagnosed with inflammatory bowel disease (IBD), and began receiving treatment from Dr. Edward Rich, a pediatric gastroenterologist at Kaiser Permanente in San Francisco. Rich Dep. at 50:5-10, 59:22-60:1, 74:23-25.[2]

Dr. Rich testified that it was not his "regular practice to look at drug labeling." Id. at 192:6-7. He received information

[2] The complete transcript of the deposition is located at Docket No. 199.

on medications from multiple sources, including meetings, other professionals in the field, articles and occasional meetings with drug representatives. Id. at 192:7-14. He explained, "Generally I'm looking at drug labeling or the PDR in medicines that I'm less familiar with." Dr. Rich could not remember whether he ever relied on labeling information for 6-MP before prescribing it to patients. Id. at 282:2-283:2.

With respect to the impact of drug labeling on his decisions regarding treatment, Dr. Rich testified, "Drug labeling is sometimes something I rely on when making decisions on drug use for patients." Id. at 190:21-23. He stated, "When I read the labeling, it's one of the things that is part of my decision-making process. Id. at 191:20-22.

Initially, Dr. Rich prescribed Prednisone, a steroid, and Asacol, an aspirin, anti-inflammatory drug, to treat Maxx's IBD. Id. at 75:8-12, 79:22-25, 82:6-8. After several months, Dr. Rich sought to wean Maxx from Prednisone, due to the significant side effects and the weakness of the drug as a long-term therapy, replacing it with 6-MP, an immunosuppressive therapy. Id. at 82:9-83:16, 86:16-22.

In June 1999, Maxx began taking 6-MP. Id. at 105:14-15. Dr. Rich prescribed varying dosages of 6-MP, while attempting to eliminate gradually Maxx's need for Prednisone. However, as of May 2002, Maxx was still taking Prednisone and 6-MP. Id. at 117:4-11.

At the time Dr. Rich prescribed 6-MP he was aware of a paper reporting the occurrence of lymphoma in adults taking the drug. Id. at 89:12-90:17. According to Dr. Rich, the frequency of lymphoma occurrences reported in the study was one in one hundred adult patients taking 6-MP. Id. at 89:23-90:4. Dr. Rich found this "significant," prompting him to warn patients of a "small but non-zero increased risk of serious infections or malignancies" when discussing 6-MP treatment with patients. Id. at 89:2-90:17. Dr. Rich testified that he may or may not have included the word "lymphoma" when providing the warning. Id. at 89:7-12.

At an appointment with Maxx on May 8, 2002, Dr. Rich discussed in detail prescribing Remicade. Id. at 117:4-118:1. Again, the goal in changing Maxx's medication at this time was to take him off steroids. Id. at 151:17-152:9. On July 10, 2002, Maxx received his first infusion of Remicade. Id. at 147:24-148:16. Maxx received infusions of Remicade approximately every three months, in combination with 6-MP. Id. at 155:4-12, 157:9, 170:12-21.

Dr. Rich considered Remicade, as well as Humira, part of a class of anti-tumor necrosis factor drugs, also known as "anti-TNF drugs" and "TNF inhibitors." Id. at 175:10-14, 176:9-17, 264:24-25, 265:2-3. He testified that he "virtually always" informed his patients of a "nonzero increased risk" of serious infections and malignancies related to "immunosuppressives and anti-tumor necrosis factor drugs." Id. at 123:6-10. Dr. Rich's notes did

not mention specific warnings as to malignancies and lymphomas, but he testified that such discussions "might not be documented." Id. at 214:5-9. Other notations indicate that he had informed Maxx of side effects.

It is not entirely clear when Dr. Rich began warning his patients about a "nonzero increased risk" of malignancies connection with Remicade. According to Dr. Rich, at a point in time he could not recall, he became aware of a study involving approximately 700 patients on Remicade therapy, a majority of whom had rheumatoid arthritis and a minority of whom had Crohn's disease. Id. at 125:13-19. The study reported incidences of serious infections and malignancies, including lymphomas, within that patient population. Id. at 125:20-126:1. An entry regarding Remicade in the 2002 Physicians' Desk Reference included mention of a clinical study involving 771 patients, seven of whom developed new or recurrent malignancies, including lymphoma. Id. at 133:2-12. However, the PDR also stated that "the observed rates and incidents [of these malignancies] were similar to those expected for the population." Id. at 133:10-12. According to Dr. Rich, in 2002 there were no reports on the risk of therapies combining Remicade and 6-MP. Id. at 132:10-12.

In about November 2005, Dr. Rich began to consider discontinuing Maxx's Remicade treatment and discussed Humira with him. Id. at 170:24-173:5. Dr. Rich also testified that in "late 2005" he became aware of a "complication" associated with

Remicade, namely the occurrence of hepatosplenic T-cell lymphoma in adolescent and young adult patients taking Remicade with 6-MP. Id. at 204:21-205:22, 215:3-4. Dr. Rich did not testify that new knowledge about "this complication" led him to consider taking Maxx off Remicade.

Maxx received an infusion of Remicade in November 2005 and then his final dose of Remicade in March 2006. Id. at 182:15-14; 197:16-199:7. In May 2006, Maxx underwent a colonoscopy that revealed no signs of IBD. Id. at 198:1-199:14. According to Dr. Rich, a decision to discontinue Remicade or use an alternative medication would have been made at the time of the colonoscopy, based on the results of the examination. Id. at 172:10-12. Maxx received no further infusions of Remicade.

Also in May 2006, the FDA approved Remicade for an additional indication for the treatment of pediatric Crohn's disease, but required a black box warning about the drug. The warning alert physicians to the following:

> RARE POSTMARKETING CASES OF HEPATOSPLENIC T-CELL LYMPHOMA HAVE BEEN REPORTED IN ADOLESCENT AND YOUNG ADULT PATIENTS WITH CROHN'S DISEASE TREATED WITH REMICADE. THIS TYPE OF T-CELL LYMPHOMA HAS A VERY AGGRESSIVE DISEASE COURSE AND IS USUALLY FATAL. ALL OF THESE HEPATOSPLENIC T-CELL LYMPHOMAS WITH REMICADE HAVE OCCURRED IN PATIENTS ON CONCOMITANT TREATMENT WITH AZATHIOPRINE OR 6-MERCAPTOPURINE.

Declaration of Kevin Haverty in Support of Plaintiffs' Opposition to GSK's Motion for Summary Judgment, Ex. 3.

Dr. Rich testified that he would have received this black box warning in the form of a letter or other notification at about the time it was issued. Rich Dep. at 214:23-215:3. However, he also noted that he had learned of this "complication" earlier, in late 2005, as previously stated.

By November 2006, Maxx experienced a relapse. On November 22, 2006, he received his first prescription for Humira, taking the drug in combination with 6-MP. Id. at 217:14-16. Dr. Rich testified that he first treated patients with Humira in early 2005 or 2006 when two sixteen year old female patients with IBD received the drug. Id. at 193:3-7; 173:19-25. Dr. Aileen Dillon, a rheumatologist, wrote Maxx's first prescription for Humira because, when Humira was first placed on the Kaiser formulary, it was placed under limited release, only through rheumatologists. Id. at 217:14-218:6. Dr. Rich testified that when he first began prescribing Humira to his patients, he warned them of a "nonzero but increased risk of serious infections and malignancies." Id. at 193:23-194:11. His awareness of this risk was based on literature he had reviewed and discussions he had had with other physicians. Id. at 194:12-18.

When asked why he did not treat Maxx with Remicade in November 2006, Dr. Rich responded,

> So in November '06, we had been aware for some time of complication of hepatosplenic T-cell lymphoma, so that would have been part of my discussion with the family. Ease of therapy is always a discussion with Humira versus Remicade.

Id. at 218:13-23. Dr. Rich explained that Humira may be administered by the patient or a family member at home through subcutaneous injections, while Remicade requires a patient to visit a facility for two to three hour infusions. Id. at 174:15-19, 267:5-23.

When asked whether he opted for Humira because of the black box warning concerning Remicade, Dr. Rich testified, "I think that the concern of hepatosplenic T-cell lymphoma would have been part of my discussion with the family and it would have been part of my thinking about the use of this disease (verbatim)." Id. at 219:16-22. Dr. Rich did not recall any similar warning regarding Humira's use in combination with 6-MP and hepatosplenic T-cell lymphoma. Id. at 219:23-220:2. Dr. Rich did not state that he would have forgone prescribing Humira in November 2006, had he learned of a black box warning or similar alert regarding the use of Humira, alone or in combination with 6-MP, and the occurrence of hepatosplenic T-cell lymphoma.

In deposition, Dr. Rich was asked whether his drug recommendation was informed by the fact that one drug had a black box warning about a rare, aggressive cancer, while the other drug did not. Dr. Rich responded,

> I don't think the black box would have been a primary driving point in the use of medicine, just as FDA indication or not is not a driving point, as FDA doesn't indicate very much of anything in pediatrics.

Id. at 220:1-15.

Later, Dr. Rich was asked again whether information that he had about the cases of hepatosplenic T-cell lymphoma associated with Remicade and 6-MP combination use informed in any way his recommendation that Maxx start Humira in November 2006. He answered,

> The occurrence of hepatosplenic T-cell lymphomas and the information and knowledge about that would have been part of many things that would have gone into my own thinking on how to use this--these medications and my discussion with the patients on how to use these medications.

Id. at 225:7-113.

In addressing whether all anti-TNF drugs carry the same risks, Dr. Rich testified that Humira was "entirely humanized," whereas Remicade was "75 percent humanized and 25 percent mouse." Id. at 194:24-25. Dr. Rich engaged in the following exchange with counsel,

> A: So I presented [anti-TNF] medications always as having an increased but nonzero increased risk. And if I was asked by a patient, "Why do you use one versus the other," or why we were considering Humira, it may have come up in discussions that Humira was fully humanized and may have--my statement would have --would have been, "It may have a better safety profile."
>
> Q: What was the basis of your thinking that it may have a better safety profile?
>
> A: That it was fully humanized.
>
> Q: What--
>
> A: That there are allergy side effects to these medicines.

> Q: Okay. Other than allergies, did the fact that Humira was fully humanized, monoclonal antibody, as opposed to Remicade, affect, in your mind, the risk of malignancies?
>
> A: I can't recall whether I thought that or not. The fact that there--I'm not an immunologist, and I'm not sure they can answer that question. But the fact that there is no mouse suggests that it might have been a consideration in my thinking, that it's a possibility.

Id. at 195:13-196:12.

Based on Dr. Rich's recommendation, Maxx took Humira for at least eight months. In mid-July 2007, Maxx was diagnosed with hepatosplenic T-cell lymphoma. In December 2007, he passed away.

After Maxx's death and as part of this litigation, Ms. Wendell testified, "I didn't know that there had been a black box warning on Remicade . . . [W]e were not informed of that and there would have been no reason for [Dr. Rich] to inform us of that because [Maxx] wasn't taking Remicade at the time." Haverty Dec., Ex. 2, Lisa Wendell Dep. at 77:4-8. Ms. Wendell recalled that Dr. Rich told her that Humira offered the convenience of self-injection and had a better safety profile. Id. at 77:9-13. The issue of convenience was considered because Maxx was moving to Davis to attend college. Id. at 76:20-24. She answered affirmatively when asked whether she would have discontinued the use of any of the medications if she had been told that there was a risk of hepatosplenic T-cell lymphoma. Id. at 75:8-12.

During 2007 Dr. Rich continued to treat patients using therapies combining anti-TNF drugs with 6-MP, although he could

not recall whether the "combination therapy" consisted of 6-MP combined with Remicade or 6-MP combined with Humira or both. Rich Dep. at 208:11-209:5. Most likely in 2008, Dr. Rich switched to using "mono-therapy," treating patients with an anti-TNF drug alone without concomitant use of 6-MP. Id. at 208:16-17, 288:13-16. Maxx's case played an "important role" in influencing Dr. Rich's decision to use monotherapy as opposed to combination therapy. Id. at 230:16-20. Dr. Rich reported that the majority of practitioners, including many pediatric gastroenterologists, use combination therapy, although that is no longer his practice. Id. at 230:12-15.

LEGAL STANDARD

Summary judgment is properly granted when no genuine and disputed issues of material fact remain, and when, viewing the evidence most favorably to the non-moving party, the movant is clearly entitled to prevail as a matter of law. Fed. R. Civ. P. 56. Celotex Corp v. Catrett, 477 U.S. 317, 322-23 (1986); Eisenberg v. Ins. Co. of N. Am., 815 F.2d 1285, 1289 (9th Cir. 1987). The court must draw all reasonable inferences in favor of the party against whom summary judgment is sought. Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 587 (1986); Intel Corp. v. Hartford Accident & Indem. Co., 952 F.2d 1551, 1558 (9th Cir. 1991).

Material facts which would preclude entry of summary judgment are those which, under applicable substantive law, may affect the

outcome of the case. The substantive law will identify which facts are material. Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986).

DISCUSSION

Under the learned intermediary doctrine, a manufacturer of a prescription drug is obliged to warn doctors, not patients, of potential side-effects associated with its pharmaceutical products. Carlin v. Superior Court, 13 Cal. 4th 1104, 1116 (1996). A plaintiff asserting causes of action for failure to warn must prove not only that no warning was provided or that the warning was inadequate, but also that the inadequacy or absence of a warning caused the plaintiff's injury. Plummer v. Lederle Laboratories, 819 F.2d 349, 358 (2d Cir. 1987) (applying California law).

Under Motus v. Pfizer, Inc., 358 F.3d 659, 661 (9th Cir. 2004), "a product defect claim based on insufficient warnings cannot survive summary judgment if stronger warnings would not have altered the conduct of the prescribing physician." In Motus the treating physician testified unequivocally that he neglected to read the published warnings and did not rely on information from Pfizer's detail men before prescribing the drug that allegedly induced the decedent to commit suicide. 385 F.3d at 661. On this basis, the plaintiff could not establish a causal connection between the representations or omissions that accompanied the product and the plaintiff's injury.

The present action is distinguishable from Motus because Dr. Rich testified that he sometimes read drug labeling, in particular when dealing with unfamiliar drugs. Although Dr. Rich learned of 6-MP during his training, there is evidence that Humira was relatively new to Dr. Rich as a treatment for IBD when he prescribed it to Maxx.

However, even assuming that Dr. Rich would have read a warning on the labels of Humira and 6-MP, summary judgment in favor of Movants is warranted. In Plummer, the Second Circuit, applying California law, found that judgment should have been entered for the defendant, because the physician knew of the risk for which the plaintiff sought a warning, and yet the physician still failed to warn the patient's mother about the risk. 819 F.2d at 358-59. Plummer, citing Rosburg v. Minnesota Mining & Mfg. Co., 181 Cal. App. 3d 726, 730 (1986), concluded that "no harm could have been caused by failure to warn of a risk already known." 819 F.2d at 359. As in Plummer, Dr. Rich knew of the risk of malignancies associated with 6-MP and Humira, but still prescribed the medication. Thus, there is insufficient evidence to create a material dispute of fact as to whether the warnings that Plaintiffs contend should have been given would have changed Maxx's treatment.

A. 6-MP

The Wendells assert that GSK, TEVA and PAR, allegedly involved in the manufacture, marketing and distribution of 6-MP,

negligently failed to discover and/or provide an adequate warning about the risk of hepatosplenic T-cell lymphoma posed by 6-MP when used singly or in combination with Remicade or Humira. Dr. Rich, however, was already aware of a significant risk of lymphomas associated with 6-MP treatment. Yet he continued to prescribe the drug. It appears that Dr. Rich's knowledge of this risk prompted him to warn his pediatric patients about the nonzero increased risk of developing malignancies or lymphomas while taking the medication, but there is no evidence that the risk persuaded him to cease recommending or prescribing the drug.

Moreover, there is insufficient evidence for a jury to infer that Dr. Rich ceased treating Maxx with Remicade because of the May 2006 black box warning regarding the risk of lymphoma associated with therapy combining Remicade and 6-MP. Dr. Rich began considering taking Maxx off Remicade in November 2005, before the black box warning was issued. In addition, he testified that black box warnings were not the driving force in making decisions about the prescription of medication. Thus, the Remicade black box warning does not provide a basis from which to infer that, had Dr. Rich received a similar warning regarding Humira and 6-MP prescribed in combination, he would have ceased treating Maxx with that combination of drugs.

Nor is there evidence that a warning specific to pediatric patients or specific to treatments combining 6-MP with TNF-blockers would have led Dr. Rich to stop prescribing 6-MP alone or

in combination with Remicade or Humira. Contrary to the Wendells' contention, evidence that Dr. Rich ceased prescribing TNF-blockers in combination with 6-MP after Maxx was diagnosed with hepatosplenic lymphoma does not prove that he would have changed his prescription practices based on the warning they suggest. A warning about rare occurrences of hepatosplenic lymphoma associated with therapy combining 6-MP and Remicade is bound to have less persuasive power than an instance of the disease affecting a doctor's own patient followed that therapy.

Because there is insufficient evidence for a reasonable jury to find that the failure to warn of the risk of hepatosplenic T-cell lymphoma posed by 6-MP when used singly or in combination with Remicade or Humira proximately caused Maxx's death, summary judgment is granted in favor of GSK, TEVA and PAR.

The Wendells also argue that it is premature to grant summary judgment in favor of GSK because further discovery may reveal that Dr. Rich relied on information from GSK concerning the risks associated with 6-MP. Apparently, GSK served a voluminous response to a request for documents, and the Wendells had not had time to sift through the discovery. However, the Wendells have not demonstrated how documents from GSK could prove proximate causation in this case, where the undisputed fact is that Dr. Rich was already aware of the risk of lymphomas associated with 6-MP, but still chose to prescribe the drug. Furthermore, Plaintiffs lack evidence that any further warning regarding the use of 6-MP,

such as a warning about its use in combination with Humira, would have changed the manner in which Dr. Rich treated Maxx. Summary judgment is not premature.

B. Humira

The Wendells claim that Abbott should have provided a label warning Dr. Rich about the risk of hepatosplenic T-cell lymphoma associated with treatment combining Humira and 6-MP. However, none of the evidence that the Wendells point to is sufficient to create a dispute of fact as to whether the warning would have altered Dr. Rich's decision to treat Maxx with Humira and 6-MP. First, for the reasons already explained above, Dr. Rich's subsequent decision to prescribe anti-TNF drugs alone, rather than in combination with 6-MP, is not probative of whether a warning about risks associated with Humira, used singly or in combination with 6-MP, would have altered Maxx's treatment.

Next, Dr. Rich's testimony regarding Humira's comparatively better safety profile is not helpful to the Wendells' case. When read in context, Dr. Rich's testimony indicates that he believed that Humira may have had a better safety profile based on the fact that it was fully humanized and, thus, had fewer allergy side effects.

Evidence that Dr. Rich did not warn Maxx about the risk of combination therapy is not sufficient to establish proximate causation with respect to Humira. Rather, Dr. Rich testified that black box warnings were not the primary driver for his decisions

regarding medication. The timing of Dr. Rich's decision to discontinue treating Maxx with Remicade is not evidence that a black box warning as to Humira would have changed the course of Maxx's treatment. Dr. Rich began considering whether to discontinue Maxx's Remicade treatment before the black box warning issued in May 2006. These grounds are insufficient to raise a dispute of fact that a warning would have made a difference in Maxx's treatment.

That Dr. Rich did not suspect Humira as a cause of Max's lymphoma after his diagnosis fails to establish that a warning about Humira would have persuaded him to stop prescribing the medication. In other words, that Dr. Rich did not associate a risk with Humira while the warning had not yet been announced does not mean that, had the warning been provided, Dr. Rich would have associated such a strong risk with Humira that he would have decided against prescribing the drug.

Furthermore, Ms. Wendell's testimony that the family would have discontinued the drug treatment if they had been warned is insufficient. Maxx was born on August 20, 1986. At the time Maxx received Humira in November 2006, he was twenty years old. There is no evidence that Ms. Wendell made health care decisions for Maxx. Ms. Wendell's statement as to what Maxx would have done lacks foundation.

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Because the Wendells have failed to provide sufficient evidence to raise a dispute of fact as to the element of proximate causation, summary judgment in favor of Abbott is warranted.

CONCLUSION

The Wendells' loss of their son is tragic. However, because they have failed to provide sufficient evidence of proximate causation by GSK, TEVA, PAR and Abbott, the motions for summary judgment submitted by these Defendants are granted. In the event that the Wendells or remaining Defendants move for summary judgment, the motions shall be noticed for January 26, 2012.

IT IS SO ORDERED.

Dated: 12/15/2011

CLAUDIA WILKEN
United States District Judge